Claims

1. Use of a secretagogue compound for the preparation of a medicament for the prophylaxis or treatment of cancer cachexia in an individual in need of such treatment.

2. The use according to claim 1, wherein the secretagogue is ghrelin or a pharmaceutically acceptable salt thereof.

3. The use according to claims 1 or 2, wherein the secretagogue is a ghrelin-like compound or a pharmaceutically acceptable salt thereof

wherein the ghrelin-like compound comprises a structure defined by formula I

$Z^1 - (X^1)_m - (X^2) - (X^3)_n - Z^2$, wherein

Z^1 is an optionally present protecting group

each X^1 is independently selected from an amino acid, wherein said amino acid is selected from naturally occurring and synthetic amino acids,

X^2 is any amino acid selected from naturally occurring and synthetic amino acids, said amino acid being modified with a bulky hydrophobic group, preferably an acyl group, or a fatty acid,

each X^3 is independently selected from an amino acid, wherein said amino acid is selected from naturally occurring and synthetic amino acids,

wherein one or more of X^1 and X^3 optionally may be modified with a bulky hydrophobic group, preferably an acyl group, or a fatty acid,

Z^2 is an optionally present protecting group,

m is an integer in the range of from 1-10

n is 0 or an integer in the range of from 1-35.

4. The use according to claim 3, wherein m is an integer in the range of from 1-9, such as of from 1-8, such as of from 1-7, such as of from 1-6, such as of from 1-5, such as of from 1-4, such as of from 1-3, such as of from 1-2, such as 2.

5. The use according to any of claims 3 or 4, wherein X^2 is selected from the group of modified Ser, modified Cys and modified Lys, such as wherein X^2 is modified Ser.

6. The use according to any of claims 3 to 5, wherein the ghrelin-like compound is selected from a compound of

formula II Z^1 – Gly- $(X^1)_{m-1}$ – (X^2) – $(X^3)_n$- Z^2,

formula III Z^1 – Gly- Ser – (X^2) – $(X^3)_n$- Z^2, and

formula IV Z^1 – Gly – (X^2) – $(X^3)_n$- Z^2.

7. The use according to claim 6, wherein the ghrelin-like compound is having formula III.

8. The use according to any of claims 6 or 7, wherein $(X^3)_n$ comprises a sequence selected from one or more of the sequences shown below:

Phe Leu Ser Pro Glu His Gln

Phe Leu Ser Pro Glu His

Phe Leu Ser Pro Glu

Phe Leu Ser Pro

Phe Leu Ser

Phe Leu

Phe

9. The use according to any of claims 3 to 8, wherein n is an integer in the range of from 1-25, such as of from 1-24, such as from 1-15, such as of from 1-10, such as of from 10-25, such as of from 10-24, such as of from 15-25, such as of from 15-24.

10. The use according to any of claims 3 to 9, wherein $(X^3)_n$ is selected from one or more of the sequences shown below:

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys Pro Pro Ala Lys Leu Gln Pro Arg

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys Pro Pro Ala Lys Leu Gln Pro

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys Pro Pro Ala Lys Leu Gln

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys Pro Pro Ala Lys Leu

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys Pro Pro Ala Lys

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys Pro Pro Ala

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys Pro Pro

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys Pro

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln

Phe Leu Ser Pro Glu His Gln Arg Val Gln

Phe Leu Ser Pro Glu His Gln Arg Val

Phe Leu Ser Pro Glu His Gln Arg

Phe Leu Ser Pro Glu His Gln

Phe Leu Ser Pro Glu His

Phe Leu Ser Pro Glu

Phe Leu Ser Pro

Phe Leu Ser

Phe Leu

Phe

11. The use according to any of claims 3 to 10, wherein the acyl group is selected from a C1-C35 acyl group, such as a C1 – C20 acyl group, such as a C1 – C15 acyl group, such as a C6 – C15 acyl group, such as a C6 – C12 acyl group, such as a C8 – C12 acyl group.

12. The use according to any of claims 3 to 11, wherein the acyl group is selected from the group of C7 acyl group, C8 acyl group, C9 acyl group, C10 acyl group, C11 acyl group, and C12 acyl group.

13. The use according to any of claims 3 to 12, wherein the acyl group is selected from the group of C8 acyl group, and C10 acyl group.

14. The use according to any of claims 3 to 13, wherein the acyl group is selected from the group of C7 acyl group, C9 acyl group, and C11 acyl group, such as from the group of C9 acyl group and C11 acyl group.

15. The use according to any of preceding claims 1 to 14, wherein the medicament is in a formulation for subcutaneous administration.

16. The use according to any of claims 1 to 15, wherein the medicament formulation comprises the secretagogue or a pharmaceutically acceptable salt thereof.

17. The use according to any of claims 15 to 16, wherein the formulation comprises the secretagogue or a salt thereof as a lyophilisate and the formulation further comprises a solvent, said lyophilisate and said solvent being in separate compartements until administration.

18. The use according to any of claims 15 to 17, wherein the formulation is a solution of the secretagogue or a salt thereof.

19. The use according to claim 17 or 18, wherein the solvent is saline.

20. The use according to any of claims 1 to 19, wherein the medicament is administered prior to or during a meal.

21. The use according to any of claims 1 to 20, wherein the medicament is administered in a concentration equivalent to from 10 ng to 10 mg ghrelin per kg bodyweight.

22. The use according to claim 21, wherein the medicament is administered in a concentration equivalent to from 0.1 μg to 1 mg ghrelin per kg bodyweight, such as from 0.5 μg to 0.5 mg ghrelin per kg bodyweight, such as from 1.0 μg to 0.1 mg ghrelin per kg bodyweight, such as from 1.0 μg to 50 μg ghrelin per kg bodyweight, such as from 1.0 μg to 10 μg ghrelin per kg bodyweight.

23. The use according to claim 22, wherein the medicament is administered in a concentration equivalent to from 0.1 μg to 1 mg ghrelin per kg bodyweight, such as from 0.5 μg to 0.5 mg ghrelin per kg bodyweight, such as from 1.0 μg to 0.1 mg ghrelin per kg bodyweight, such as from 1.0 μg to 50 μg ghrelin per kg bodyweight, such as from 1.0 μg to 10 μg ghrelin per kg bodyweight.

24. The use according to any of claims 1 to 23, wherein the medicament is administered as a bolus prior to or during a meal, said bolus comprising an amount of the ghrelin-like compound or a salt thereof equivalent to from 0.3 μg to 600 mg ghrelin

25. The use according to claim 24, wherein the medicament is administered as a bolus prior to or during a meal, said bolus comprising an amount of the ghrelin-like compound or a salt thereof equivalent to from 2.0 μg to 200 mg ghrelin, such as from 5.0 μg to 100 mg ghrelin, such as from 10 μg to 50 mg ghrelin, such as from 10 μg to 5 mg ghrelin, such as from 10 μg to 1.0 mg ghrelin.

26. The use according to any of claims 1 to 25, wherein the medicament is administered from one to three times daily, each administration being during a meal or at the most 180 minutes prior to a meal, such as at the most 90 minutes prior to a meal, e.g. at the most 45 minutes prior to a meal, such as at the most 30 minutes prior to a meal, such as at the most 25 minutes prior to a meal, such as at the most 20 minutes prior to a meal, such as at the most 15 minutes prior to a meal, such as at the most 10 minutes prior to a meal, such as at the most 5 minutes prior to a meal.

27. The use according to claim 26, wherein the medicament is administered three times daily.

28. The use according to any of claims 1 to 27, wherein the cancer cachexia is caused by a catabolic disorder.

29. The use according to any of claims 1 to 27, wherein the cancer cachexia is caused by an anorectic disorder.

30. The use according to any of claims 1 to 28, where the individual is suffering from a cancer selected from lung cancer, pancreatic cancer, liver cancer, and GI tract cancers.

31. Use according to any of claims 1 to 30, wherein said medicament is administered in combination with a chemotherapy medicament.

32. The use according to any of claims 1-31, wherein the treatment or prevention of cancer cachexia leads to stimulation of appetite, stimulation of food intake, stimulation of weight gain or weight maintenance, and/or increased body fat mass.

33. A method for preventing or treating cancer cachexia, comprising administering to an individual in need thereof an effective amount of a secretagogue as defined in any of claims 2-14.

34. A method for preventing or treating cancer, comprising administering to an individual in need thereof an effective amount of a secretagogue as defined in any of claims 2-14, in combination with an anti-neoplastic treatment.

35. The method according to claim 34, wherein the antineoplastic treatment is radiotherapy.

36. The method according to claim 34, wherein the antineoplastic treatment is chemotherapy.

37. The method according to any of claims 33-36, wherein the treatment or prevention of cancer cachexia leads to stimulation of appetite, stimulation of food intake, stimulation of weight gain or weight maintenance, and/or increased body fat mass.

38. Use of a ghrelin-like compound or a pharmaceutically acceptable salt thereof for the preparation of a medicament for prophylaxis or treatment of cachexia in an individual by administering a subcutaneous dosage of said medicament to the individual,

wherein the ghrelin-like compound comprises a structure defined by formula I

$Z^1 - (X^1)_m - (X^2) - (X^3)_n - Z^2$, wherein

Z^1 is an optionally present protecting group

each X^1 is independently selected from an amino acid, wherein said amino acid is selected from naturally occurring and synthetic amino acids,

X^2 is any amino acid selected from naturally occurring and synthetic amino acids, said amino acid being modified with a bulky hydrophobic group, preferably an acyl group, or a fatty acid,

each X^3 is independently selected from an amino acid, wherein said amino acid is selected from naturally occurring and synthetic amino acids,

wherein one or more of X^1 and X^3 optionally may be modified with a bulky hydrophobic group, preferably an acyl group, or a fatty acid,

Z^2 is an optionally present protecting group,

m is an integer in the range of from 1-10

n is 0 or an integer in the range of from 1-35.

39. Use according to claim 38, wherein the ghrelin-like compound is as defined in any of claims 4-14.

40. Use according to claim 38 or 39, wherein the medicament is in a formulation for subcutaneous administration.

41. Use according to claim 40, wherein the formulation comprises the ghrelin-like compound or a pharmaceutically acceptable salt thereof.

42. Use according to any of the preceding claims 40 or 41, wherein the formulation
comprises the ghrelin-like compound or a salt thereof as a lyophilisate and the formulation further comprises a solvent, said lyophilisate and said solvent being in separate compartements until administration.

43. Use according to any of the preceding claims 40 or 41, wherein the formulation is a solution of the ghrelin-like compound or a salt thereof.

44. Use according to claim 42 or 43, wherein the solvent is saline.

45. Use according to any of the preceding claims, wherein the medicament is administered as defined in any of claims 20-27.

46. Use according to any of claims 38 to 45, wherein the medicament is ad ministered from one to three times daily, each administration being prior to or during a meal, preferably less than 180 minutes prior to a meal, such as less than 90 minutes prior to a meal, for example less than 45 minutes prior to a meal, such as less than 30 minutes prior to a meal, for example less than 25 minutes prior to a meal, such as less than 20 minutes prior to a meal, for example less than 15 minutes prior to a meal, such as about 10 minutes prior to a meal, for example about 5 minutes prior to a meal, such as immediately prior to a meal, or during a meal, such as less than 90 minutes after commencing a meal, for example less than 45 minutes after commencing a meal, such as less

than 30 minutes after commencing a meal, for example less than 25 minutes after commencing a meal, such as less than 20 minutes after commencing a meal, for example less than 15 minutes after commencing a meal, such as less than 10 minutes after commencing a meal, for example less than 5 minutes after commencing a meal.

47. Use according to claim 46, wherein the medicament is administered from one to three times daily, preferably once prior to or during breakfast and/or once prior to or during lunch and/or once prior to or during dinner.

48. A ghrelin-like compound wherein the ghrelin-like compound is defined by formula I

$Z^1 - (X^1)_m - (X^2) - (X^3)_n - Z^2$, wherein

Z^1 is an optionally present protecting group

each X^1 is independently selected from an amino acid, wherein said amino acid is selected from naturally occurring and synthetic amino acids,

X^2 is any amino acid selected from naturally occurring and synthetic amino acids, said amino acid being modified with an acyl group, wherein the acyl group is selected from the group of C7 acyl group, C9 acyl group, and C11 acyl group, such as from the group of C9 acyl group and C11 acyl group.

each X^3 is independently selected from an amino acid, wherein said amino acid is selected from naturally occurring and synthetic amino acids,

Z^2 is an optionally present protecting group,

wherein one or more of X^1 and X^3 optionally may be modified by a bulky hydrophobic group, preferably an acyl group, or a fatty acid,

m is 0 or an integer in the range of from 1-10

n is 0 or an integer in the range of from 1-35.

49. The compound according to claim 48, wherein m is an integer in the range of from 1-9, such as of from 1-8, such as of from 1-7, such as of from 1-6, such as of from 1-5, such as of from 1-4, such as of from 1-3, such as of from 1-2, such as 2.

50. The compound according to any of claims 48 and 49, wherein X^2 is selected from the group of modified Ser, modified Cys and modified Lys, such as wherein X^2 is modified Ser.

51. The compound according to any of the claims 48 to 50, wherein the ghrelin-like compound is selected from a compound of

formula II Z^1 – Gly- $(X^1)_{m-1}$ – (X^2) – $(X^3)_n$- Z^2,

formula III Z^1 – Gly- Ser – (X^2) – $(X^3)_n$- Z^2, and

formula IV Z^1 – Gly – (X^2) – $(X^3)_n$- Z^2.

52. The compound according to claim 51, wherein the ghrelin-like compound is having formula III.

53. The compound according to any of claims 48 to 52, wherein n is an integer in the range of from 1-25, such as of from 1-24, such as from 1-15, such as of from 1-10, such as of from 10-25, such as of from 10-24, such as of from 15-25, such as of from 15-24.

54 The compound according to any of claims 48 to 53, wherein $(X^3)_n$ comprises a sequence selected from one or more of the sequences shown below:

Phe Leu Ser Pro Glu His Gln

Phe Leu Ser Pro Glu His

Phe Leu Ser Pro Glu

Phe Leu Ser Pro

Phe Leu Ser

Phe Leu

Phe

55. The compound according to any of claims 48 to 54, wherein $(X^3)_n$ is selected from one or more of the sequences shown below:

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys Pro Pro Ala Lys Leu Gln Pro Arg

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys Pro Pro Ala Lys Leu Gln Pro

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys Pro Pro Ala Lys Leu Gln

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys Pro Pro Ala Lys Leu

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys Pro Pro Ala Lys

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys Pro Pro Ala

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys Pro Pro

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys Pro

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys Lys

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser Lys

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu Ser

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys Glu

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg

Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln

Phe Leu Ser Pro Glu His Gln Arg Val Gln

Phe Leu Ser Pro Glu His Gln Arg Val

Phe Leu Ser Pro Glu His Gln Arg

Phe Leu Ser Pro Glu His Gln

Phe Leu Ser Pro Glu His

Phe Leu Ser Pro Glu

Phe Leu Ser Pro

Phe Leu Ser

Phe Leu

Phe

56. A pharmaceutical composition comprising the ghrelin-like compound as defined in any of the claims 48 to 55 or a pharmaceutically acceptable salt thereof and pharmaceutically acceptable carriers, vehicles and/or excipients.

57 The pharmaceutical composition according to claim 56, wherein said composition further comprises transport molecules, such as liposomes, micelles, iscoms, and/or microspheres.

58. The pharmaceutical composition according to any of claims 56 to 57, comprising a secretagogue conjugate.

59. The pharmaceutical composition according to claim 58, wherein said conjugate is comprised of a secretagogue conjugated to one or more of:

a) a polymer molecule
b) an oligosaccharide moiety
c) the Fc region of an IgG

60. A medical packaging comprising one or more dosage units of the pharmaceutical composition as defined in any of claims 56 to 59.

61. The medical packaging according to claim 60, said packaging comprising from one to three dosage units.

62. The medical packaging according to claim 61, having three dosage units.

63. The medical packaging according to claim 60, said packaging having from 7 to 21 dosage units.

64. The medical packaging according to any of the claims 60 to 63, wherein said dosage unit comprises an amount of the ghrelin-like compound or a salt thereof equivalent to from 0.3 μg to 600 mg ghrelin, such as of from 2.0 μg to 200 mg ghrelin, such as from 5.0 μg to 100 mg ghrelin, such as from 10 μg to 50 mg ghrelin, such as from 10 μg to 5 mg ghrelin, such as from 10 μg to 1.0 mg ghrelin.

65. The medical packaging according to any of the claims 60 to 64, comprising instructions for administering the pharmaceutical composition.

66. The medical packaging according to claim 65, wherein said instructions include instructions referring to administration of said pharmaceutical composition during a meal or at the most 180 minutes prior to a meal, such as at the most 90 minutes prior to a meal, such as at the most 45 minutes prior to a meal, such as at most 30 minutes prior to a meal, such as at the most 25 minutes prior to a meal, such as at the most 20 minutes prior to a meal, such as at the most 15 minutes prior to a meal, such as at the most 10 minutes prior to a meal, such as at the most 5 minutes of a meal, such as immediately prior to a meal.

67. The medical packaging according to any of claims 60 to 66, wherein the packaging is in the form of a cartridge, such as a cartridge for an injection pen.

68. Use of the ghrelin-like compound as defined in any of claims 48 to 55, or a pharmaceutically acceptable salt thereof, for the preparation of a medicament for the treatment of an individual in need thereof.

69. The use according to claim 68, wherein said medicament is in a formulation for subcutaneous administration.

70. The use according to any of claims 68 or 69, wherein the medicament comprises the ghrelin-like compound or a salt thereof as a lyophilisate and the medicament further comprises a solvent, said lyophilisate and said solvent being in separate compartements until administration.

71. The use according to any of the preceding claims 68 to 70 wherein the medicament comprises a solution of the ghrelin-like compound or a salt thereof.

72. The use according to claim 70 or 71, wherein the solvent is saline.

73. The use according to any of claims 68 to 72, wherein the medicament is administered before a meal or during the intake of a meal as defined in any of claims 45-47.

74. A method for monitoring the effect of a treatment of an individual with a secretagogue, comprising measuring the blood level in said individual of IGF-1, IGFBP-3, and/or ALS.

75. A method for preventing or treating cachexia, comprising administering to an individual in need thereof an effective amount of a secretagogue and an effective amount of a NSAID medicament.

76. The method according to claim 75, wherein the secretagogue is as defined in any of claims 2 to 14.

77. Use of a ghrelin-like compound or a pharmaceutically acceptable salt thereof for the preparation of a medicament for stimulation of appetite in an individual by administering a subcutaneous dosage of said medicament to the individual,

wherein the ghrelin-like compound comprises a structure defined by formula I

$Z^1 - (X^1)_m - (X^2) - (X^3)_n - Z^2$, wherein

Z^1 is an optionally present protecting group

each X^1 is independently selected from an amino acid, wherein said amino acid is selected from naturally occurring and synthetic amino acids,

X^2 is any amino acid selected from naturally occurring and synthetic amino acids, said amino acid being modified with a bulky hydrophobic group, preferably an acyl group, or a fatty acid,

each X^3 is independently selected from an amino acid, wherein said amino acid is selected from naturally occurring and synthetic amino acids,

wherein one or more of X^1 and X^3 optionally may be modified with a bulky hydrophobic group, preferably an acyl group, or a fatty acid,

Z^2 is an optionally present protecting group,

m is an integer in the range of from 1-10

n is 0 or an integer in the range of from 1-35.

78. Use according to claim 77, wherein the ghrelin-like compound is as defined in any of claims 4-14.

79. Use according to claim 77 or 78, wherein the medicament is in a formulation for subcutaneous administration.

80. Use according to claim 79, wherein the formulation is as defined in any of claims 41 or 42.

81. Use according to claim 80, wherein the solvent is saline.

82. Use according to any of claims 77 to 81, wherein the medicament is administered as defined in any of claims 45-47.